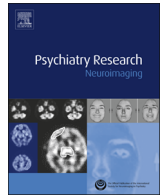




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Review article

Rostral medial prefrontal dysfunctions and consummatory pleasure in schizophrenia: A meta-analysis of functional imaging studies

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ABSTRACT

A large number of imaging studies have examined the neural correlates of consummatory pleasure and anticipatory pleasure in schizophrenia, but the brain regions where schizophrenia patients consistently demonstrate dysfunctions remain unclear. We performed a series of meta-analyses on imaging studies to delineate the regions associated with consummatory and anticipatory pleasure dysfunctions in schizophrenia. Nineteen functional magnetic resonance imaging or positron emission tomography studies using whole brain analysis were identified through a literature search (PubMed and EBSCO; January 1990–February 2014). Activation likelihood estimation was performed using the GingerALE software. The clusters identified were obtained after controlling for the false discovery rate at $p < 0.05$ and applying a minimum cluster size of 200 mm^3 . It was found that schizophrenia patients exhibited decreased activation mainly in the rostral medial prefrontal cortex (rmPFC), the right parahippocampus/amygala, and other limbic regions (e.g., the subgenual anterior cingulate cortex, the putamen, and the medial globus pallidus) when consummating pleasure. Task instructions (feeling vs. stimuli) were differentially related to medial prefrontal dysfunction in schizophrenia. When patients anticipated pleasure, reduced activation in the left putamen was observed, despite the limited number of studies. Our findings suggest that the medial prefrontal cortex and limbic regions may play an important role in neural dysfunction underlying deficits in consummatory pleasure in schizophrenia.

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1. Introduction

Anhedonia, defined as the inability to experience pleasure, is a core feature of negative symptoms in schizophrenia (Andreason, 1983; Pelizza and Ferrari, 2009). Functional imaging studies have provided researchers the opportunity to examine the neural correlates associated with hedonic experience in schizophrenia (Knutson and Greer, 2008; Kringsbach and Berridge, 2009). Pleasure experience is widely accepted as a construct involving two distinct components, anticipatory pleasure (defined as the emotional state in anticipation of future pleasurable events) and consummatory pleasure (defined as the emotional state while experiencing pleasurable events) (Gard et al., 2006; Knutson and Greer, 2008; Kringsbach and Berridge, 2009). Different brain regions have been proposed to be responsible for these two components (Knutson and Greer, 2008; Kringsbach and Berridge, 2009). Specifically, the ventral striatum (VS) and the ventral tegmental area (VTA) are thought to be primarily responsible for anticipatory (Berridge and Robinson, 1998; de Haan et al., 2004; Knutson and Greer, 2008), while the medial prefrontal cortex (mPFC) and the amygdala are thought to be associated with consummatory pleasure (Knutson et al., 2003; Knutson and Greer, 2008).

For consummatory pleasure, the findings in previous imaging studies provided a mixed picture of mPFC and amygdala activation in schizophrenia patients (Crespo-Facorro et al., 2001; Paradiso et al., 2003; Schlagenhauf et al., 2009; Waltz et al., 2009; Dowd and Barch, 2010; Ursu et al., 2011). For example, some studies reported that patients with schizophrenia exhibited reduced activation in the mPFC in response to the delivery of juice (Waltz et al., 2009), pleasurable odour (Crespo-Facorro et al., 2001) and positive pictures (Paradiso et al., 2003). However, Dowd and Barch (2010) did not find this impairment in schizophrenia patients who viewed positively valenced pictures, faces and words. Likewise, several imaging studies reported that patients with schizophrenia exhibited attenuated activation in bilateral amygdala when they were presented with pictures of happy faces and pleasurable odours (Gur et al., 2002; Schneider et al., 2007; Gradin et al., 2011). However, two other studies found enhanced activation in bilateral amygdala in patients with schizophrenia during the processing of positive affective pictures (Paradiso et al., 2003; Reske et al., 2007).

For anticipatory pleasure, more and more studies in recent years have examined striatal activation associated with the expectation of positive events in patients with schizophrenia. Previous imaging studies in clinical samples suggest that when compared with healthy controls, patients with schizophrenia showed decreased ventral striatal activation in anticipation of reward (Juckel et al., 2006a, 2006b; Schlagenhauf et al., 2008, 2009). Another imaging study reported reduced activation in the dorsal striatum (i.e., the putamen) when schizophrenia patients were

presented with unexpected juice deliveries (Waltz et al., 2009). However, these findings have not always been consistent. Some studies only reported reduced activation in the unilateral ventral striatum (left or right) (Juckel et al., 2006a, 2006b; Schlagenhauf et al., 2008) in schizophrenia patients relative to healthy controls. Another study has suggested reduced activation in bilateral ventral striatum in schizophrenia (Schlagenhauf et al., 2009). One study found enhanced activation in this region (Gradin et al., 2011) during expectation of rewarding stimuli. However, other studies did not find any difference in ventral striatal activation between schizophrenia patients and healthy controls (Walter et al., 2009; Simon et al., 2010; Waltz et al., 2010).

To the best of our knowledge, although there have been several recent narrative reviews on the neural mechanism of hedonic experience in patients with schizophrenia (Andreasen et al., 1997; Abler et al., 2008; Craig, 2009; Barch and Dowd, 2010; Kringsbach and Caponigro, 2010), few meta-analyses have been carried out to quantitatively examine the neural correlates associated with hedonic experience. For example, the question of whether there exist brain regions consistently reflecting impairment in response to positive stimuli in schizophrenia is unresolved. Furthermore, we know little about the exact neural basis of anticipatory and consummatory pleasure dysfunction in schizophrenia (Kring and Barch, 2014). One recent meta-analysis demonstrated that patients with schizophrenia showed reduced activation in response to emotional experience in the left occipital pole compared with healthy controls (Taylor et al., 2012). However, the authors mainly focused their attention on negative emotions rather than positive emotions, and hedonic experience, which may be elicited by reward stimuli (Knutson and Greer, 2008; Kringsbach and Berridge, 2009), was not investigated. Therefore, in the present study, we aimed to perform an objective, systematic and quantitative analysis of the imaging literature using activation likelihood estimation (ALE) to investigate the neural correlates of anticipatory and consummatory pleasure in schizophrenia.

Meanwhile, since different tasks and stimuli were used and different types of patients (e.g., with regard to medication status and severity of negative symptoms) were recruited in different studies, we have further examined whether these confounding factors affected the ALE findings.

2. Methods

2.1. Selection of articles

PubMed and EBSCO (PsycARTICLES, PsycINFO, PsycEXTRA, PsycCRITIQUES) online database searches were conducted between January 1990 and February 2014. Search terms included "emotion," "emotional experience," "affective experience," "pleasure," "anhedonia", "positive emotion", "positive affect", "reward", and

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